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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Sharlene Adams et al.
Serial No.:	10/616,409
Confirmation No.:	9289
Filed:	July 9, 2003
For:	BOROPROLINE COMPOUND COMBINATION THERAPY
Examiner:	Brandon J. Fetterolf
Art Unit:	1642

CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)

The undersigned hereby certifies that this document is being placed in the United States mail with first-class postage attached, addressed to MAIL STOP AMENDMENT, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on April 21, 2006.

MAIL STOP AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

DECLARATION OF MARGARET J. UPRICHARD UNDER 37 CFR §1.132

I, Margaret J. Uprichard, declare as follows:

1. I am a Senior Vice President and the Chief Development Officer at Point Therapeutics, Inc. Point Therapeutics, Inc. is the sole assignee of the above-identified application. My curriculum vitae is attached to this Declaration as Appendix A. I am also a co-presenter of the attached poster which was presented at the American Society of Hematology Annual Meeting in December 2005. I make this Declaration in support of the Amendment filed in connection with the above-identified application, and in response to the Office Action dated October 21, 2005.

2. This Declaration describes the results of a Phase II clinical trial sponsored by Point Therapeutics, Inc. The results relate to anti-tumor responses observed in human subjects who received Talabostat (i.e., Val-boroPro, PT-100) and the anti-CD20 antibody rituximab. Talabostat is an agent of Formula I, as recited in the pending claims of the above-identified application.

3. The clinical trial related to the combined use of Talabostat and rituximab in patients with advanced chronic lymphocytic leukemia. Subjects were eligible for the trial if they had primary resistance to a fludarabine or rituximab-containing regimen (i.e., no partial or complete response observed) or if they had progressive disease within one year of a prior response to either treatment. Subjects were treated as shown in the poster. Briefly, the treatment regimen was a 28-day cycle that consisted of administration of rituximab on days 1, 8, 15 and 22 and twice a day administration of Talabostat on days 2-7, 9-14, 16-21 and 23-28. Patients were observed for disease response, duration, progression-free survival and survival. Objective responses were observed in five subjects who had failed a prior rituximab regimen.

4. The clinical trials were conducted in a manner consistent with the description in the above-identified application. For example, the application teaches treatment of human subjects (page 61 line 17) having chronic lymphocytic leukemia (page 5 line 19 and [0041]) using Talabostat (page 5 line 6) in conjunction with an anti-CD20 antibody such as rituximab (page 9 line 33). In particular, the application describes that a Formula I agent (e.g., Talabostat) can be used to enhance the efficacy of disease specific antibodies including anti-cancer antibodies thereby providing an unexpected benefit over the administration of either agent alone (page 2 lines 13-16 and 25-27 and page 50 line 13-17). The application further describes treatment of subjects having refractory cancer (page 5 line 28). The application also describes a treatment regimen that involves administration of an antibody on day one of a seven day cycle followed by twice daily administration of a Formula I agent for the remaining six days of the cycle (page 11 line 8-11), and it further contemplates performing the cycle four times resulting in a 28 day treatment regimen (page 11 line 12).

5. These results show that Talabostat enhanced the activity of rituximab in patients with B-cell malignancies who had failed a prior rituximab regimen. These results correlate with and are supportive of the invention as described in the above-identified application and as claimed.

6. The ability of Formula I agents such as Talabostat to enhance the anti-cancer effect of an antibody such as an anti-CD20 antibody could not have been predicted and thus was unexpected

prior to the invention.

7. I, the undersigned, declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true. And further, that the statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of title 18 of the United States code and that such willful false statements may jeopardize the validity of this document and any patent which may issue from the above-identified patent application.

21 Apr 2006
Date

Margaret J. Uprichard, PharmD.
Senior Vice President, Chief Development Officer
Point Therapeutics, Inc.
155 Federal Street, 4th Floor
Boston, Massachusetts 02110-1727

American Society of Hematology
Annual Meeting - December 2005

2125: Phase 2 Study of Talabostat and Rituximab in Patients with Advanced CLL Previously Treated with Rituximab/Fludarabine

Khuda D Khan, MD, PhD[1], Susan O'Brien, MD[2], Kanti R Rai, MD[3], Jennifer R Brown, MD, PhD[4], Perry Cook, MD[5], Anne-Marie Maddox, MD[6], Camille Abboud, MD[7], Alison M Duarte, MPH[8], Zejiang Yang[9], Eric J Haltom[8], and Margaret J Uprichard, PharmD[8]. [1]Indiana Oncology Hematology Consultants, Indianapolis, IN; [2]MD Anderson Cancer Center, Houston, TX; [3]Long Island Jewish Medical Center, New Hyde Park, NY; [4]Dana-Farber Cancer Institute, Boston, MA; [5]New York University Medical Center, New York, NY; [6]University of Arkansas for Medical Science, Little Rock, AR; [7]James P. Wilmot Cancer Center, Rochester, NY; [8]Point Therapeutics, Boston, MA; [9]Kendle International Inc, Cincinnati, OH

Introduction

Talabostat is an orally administered small molecule that inhibits dipeptidyl peptidases such as CD26 and fibroblast activation protein (FAP). FAP is expressed in bone marrow, lymph nodes, and the stroma of solid tumors, and CD26 has been shown to be abnormally expressed in B-CLL. Talabostat induces the production of cytokines and chemokines in lymph nodes and spleen, stimulating both adaptive and innate immune responses. Talabostat was shown to enhance the activity of rituximab in a Phase 1 study in patients with B-cell malignancies who had failed rituximab, most likely by enhancing the antibody-dependent cell-mediated cytotoxicity of rituximab.

Study Objectives

This Phase 2 trial was conducted to determine the efficacy (response rate) of talabostat in combination with rituximab in patients with advanced CLL who failed a fludarabine/rituximab regimen.

Study Design

- Single-arm, open label, multi-center study in up to 54 evaluable patients
- Treatment regimen (28-day treatment course)
  - Rituximab 375mg/m^2 intravenously weekly x 4 weeks (Study Days 1, 8, 15, 22)
  - Talabostat 300µg tablets BID on Study Days 2-7, 9-14, 16-21, and 23-28
  - Additional courses permitted depending on tolerability and response
- Outcome measures
  - Primary: Disease response (evaluated per NCI-WG criteria)
  - Secondary: Response duration, progression-free survival, and survival
- Adverse events coded using MedDRA and severity assessed using NCI-CTCAE
- Patients followed for 12 months for survival and disease progression (PD)

Methods

Eligibility Criteria

- Men or women age ≥18 years
- Histopathologically confirmed diagnosis of B-CLL expressing surface CD20 of any detectible intensity
- Rai Stage III or IV (or Rai Stages I and II with massive or progressive lymphadenopathy or hepatosplenomegaly)
- Primary resistance (no PR or CR) to a fludarabine regimen or PD within 1 year of a prior response
- ECOG PS 0, 1, or 2
- No CNS metastases
- Baseline laboratory results within the following parameters:
  - Serum creatinine ≤2.0mg/dL
  - AST or ALT < 3 x the upper limit of normal (ULN)
  - Total bilirubin < 1.5 x ULN (unless secondary to Gilbert's)
- No history of hepatitis B or C
- No chemotherapy, radiation, biologic, or immunotherapy within 4 weeks of Study Day 1

Results

Patient Population

To date, 36 patients have entered this study. The median age is 63.5 years (range 42 to 83), and the majority (80.6%) of patients are men. Most patients (83.3%) are Caucasian, and 66.7% were Rai Stage IV. Median baseline WBC was 10.2 x 10^3/µL (range 2.5 to 264.4) and the median lymphocyte percentage was 70.0% (range 7.0 to 93.0). The majority of patients (77.8%) have been treated previously with a rituximab regimen, and 33.3% had also received alemtuzumab.

Patient Demographics
(N=36)

Age (years)	
Mean (SD)	64.7 (10.7)
Median	63.5
Range	42–83
Gender n (%)	
Male	29 (80.6)
Female	7 (19.4)
Race n (%)	
White, non-Hispanic	30 (83.3)
Black, non-Hispanic	5 (13.9)
Other	1 (2.8)
ECOG n (%)	
0	14 (38.9)
1	17 (47.2)
2	5 (13.9)
Rai Stage n (%)	
Stage I	7 (19.4)
Stage II	2 (5.6)
Stage III	3 (8.3)
Stage IV	24 (66.7)
Serum β2 Microglobulin (mg/L)	
Mean (SD)	6.5 (4.7)
Median (Range)	4.9 (1.7-22.5)
Number of Prior Regimens	
Mean	4
Median (Range)	4 (1-10)
Prior Rituximab n (%)	
Yes	28 (77.8)
No	8 (22.2)
Prior Alemtuzumab n (%)	
Yes	12 (33.3)
No	24 (66.7)

Note: Data are preliminary

Clinical Disease Assessments

Of the 36 patients enrolled, 31 meet criteria for evaluability (at least 6 days of talabostat with a post-baseline response assessment by the investigator). Investigators have reported clinical responses in 7 of 31 evaluable patients (22.5%). Five of 7 patients had received prior rituximab.

Objective Response

Age/Sex	Response	Duration of Response (months)	Prior Rituximab	# Prior Tx Regimens	Time Since Prior Regimen (months)	Best Response to Prior Regimen
63/M	PR	5	Yes#	4	2.5	PD
50/F	PR	9*	Yes	3	15	SD
77/F	PR	5*	No	2	2.7	PD
75/M	PR	5*	No	2	9	SD
80/M	PR	4.5	Yes#	9	3	PD
61/M	PR	1**	Yes#	8	2	SD
42/M	PR	2*	Yes	2	4	PD

* Response continuing ** Awaiting confirmatory assessment # Prior Alemtuzumab
Note: data are preliminary

Three patients had also progressed on alemtuzumab. Median PFS and survival are not yet estimated due to the fact that the study is ongoing and data are still preliminary.

The mean number of courses patients have received is 1.6. Most patients (61.1%) have received at least 1 course of treatment (range 0.2 to 9); 8 patients have receive ≥ 2 courses.

Conclusions

- The combination of talabostat and rituximab shows promising activity in patients with advanced CLL who have failed prior fludarabine/rituximab
- The partial response rate in evaluable patients is currently 22.5% in this ongoing study
- Five of 7 PRs were observed in patients who failed prior rituximab. Three of these patients had also failed alemtuzumab.
- The most frequent adverse events are those commonly reported with rituximab, with the exception of peripheral edema
- The trial is still enrolling, and patients are being followed for durability of response, progression-free survival, and survival

This trial is partially funded through an Orphan Products Grant (FD-R-003021-01) from the Food and Drug Administration, Office of Orphan Products Development.

Safety and Tolerability

The most frequently reported adverse events (all toxicity grades) are nausea and pyrexia (each at 27.8%), peripheral edema (25.0%), dyspnea (19.4%), fatigue and pruritis (16.7%, each). Four patients died during the study due to CLL or related complications.

Grade 3 and 4 Adverse Events
(N=36)

System Organ Class/Preferred Term	All Grades	Grade 3	Grade 4
Blood and Lymphatic System Disorders			
Febrile neutropenia	4 (11.1)	2 (5.6)	1 (2.8)
Neutropenia	2 (5.6)	1 (2.8)	0
Platelet count decreased	1 (2.8)	0	1 (2.8)
General Disorders and Administration Site Conditions			
Fatigue	6 (16.7)	2 (5.6)	0
Pyrexia	10 (27.8)	1 (2.8)	0
Infections and Infestations			
Fungal infection	2 (5.6)	2 (5.6)	0
Cellulitis	1 (2.8)	1 (2.8)	0
Pneumonia NOS	1 (2.8)	1 (2.8)	0
Metabolism and Nutrition Disorders			
Acidosis	1 (2.8)	1 (2.8)	0
Hyperglycemia	1 (2.8)	1 (2.8)	0
Hypocalcemia	1 (2.8)	1 (2.8)	0
Hypoglycemia	1 (2.8)	0	1 (2.8)
Musculoskeletal and Connective Tissue Disorders			
Pain in extremity	1 (2.8)	1 (2.8)	0
Nervous System Disorders			
Dizziness	3 (8.3)	1 (2.8)	0
Psychiartic Disorders			
Insomnia	2 (5.6)	1 (2.8)	0
Respiratory, Thoracic and Mediastinal			
Dyspnea	7 (19.4)	3 (8.3)	0
Pulmonary embolism	1 (2.8)	0	1 (2.8)
Surgical and Medical Procedures			
Wound debridement	1 (2.8)	1 (2.8)	0

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KHAN *et al.*, "Phase 2 Study of Talabostat and Rituximab in Patients with Advanced CLL Previously Treated with Rituximab/Fludarabine." American Society of Hematology Annual Meeting. December 2005. Poster 2125.

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Pulmonary embolism	1 (2.8)	0	1 (2.8)
Surgical and Medical Procedures			
Wound debridement	1 (2.8)	1 (2.8)	0

Note: data are preliminary

Margaret J. Uprichard, PharmD

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Sherborn, MA 01770
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Home: (508) 647-0706
Mobile: (508) 333-1228
Fax: (508) 647-5166

Summary of Qualifications

Synopsis

A Pharmaceutical Executive with more than 16 years experience in Drug and Biologics Development, both in large pharmaceutical and small biotechnology companies. Current position is Sr. Vice President, Chief Development Officer, for a small public Biotechnology company. Dynamic, high-energy, innovative, goal-oriented thinker with a common sense and sound judgment. Prior positions include Sr. Vice President, Drug Development, Vice President of Clinical Affairs, Worldwide Regulatory Affairs, and Preclinical Development in both US and German Biotechnology companies. Strong leadership, management and team-building skills. Collaborative management style and documented success in directing teams of professionals in diverse disciplines and managing external resources in the product development process. Career foundation comprises 11 years in large Pharma and 6 years biotechnology including entrepreneurial, start-up environments.

Professional Experience

Point Therapeutics, Inc — January 2003 – Present

A Biotechnology company dedicated to the research of cancer and chemotherapy-related disorders.

Sr. Vice President, Chief Development Officer *(2005)*
Sr. Vice President, Drug Development *(2004)*
Sr. Vice President, Clinical and Regulatory Affairs *(2003)*

- Effectively spearhead drug development and effectively manage and lead key disciplines including Clinical and Regulatory Affairs, Project Management, Toxicology, Pharmacokinetics and Drug Metabolism, and Manufacturing
- Establish regulatory and clinical strategy involving evaluating creative opportunities to allow for the most effective and efficient route to drug approval
- Develop and execute development strategy from preclinical proof-of-concept to registration for small molecules
- Develop and implement integrated development program plans identifying all critical path activities, established go/no-go decision points, budgets and manage costs
- Member of the Executive Management Team reporting to CEO
- Key involvement in potential partnering activities, including presenting company plan and vision to scientific, clinical, regulatory, and business development
- Present company vision and development strategy to potential investors
- Provide critical scientific, clinical, and regulatory assessment of potential in-licensing and business opportunities for integration into current company portfolio

Uprichard Consulting, LLC May 2001-2003
Independent consultant to the Biotechnology sector providing leadership and strategic advice on drug and biologics research and development.

Acting Vice-President, Clinical and Regulatory Affairs
Curis, Inc.
Cambridge, MA *(May 2001-December 2002)*

- Developed regulatory and clinical strategy for two cell therapy compounds
- Restructured Clinical organization to enable effective execution of clinical strategy; eight direct reports included one MD Director and below
- Established and led a cross-functional team including preclinical, clinical, regulatory, manufacturing, quality assurance and marketing
- Identified resource constraints and bottlenecks to development and devised solutions and revised assumptions
- Member of Senior Management Team; involved in partnering activities
- Established Preclinical, Clinical, and Regulatory worldwide registration strategies for two separate therapeutic collaborations

Head, Worldwide Regulatory Affairs and Preclinical Development
PAION GmbH
Aachen Germany *(February 2002-October 2002)*

- Developed worldwide regulatory strategy for registration of in-licensed small molecules and proteins to treat stroke
- Responsible for directing preclinical activities (pharmacology and toxicology) and outsourcing and assuring that preclinical studies were consistent with regulatory standards
- Head of interim US office responsible for execution of US clinical development activities; responsible for evaluating the possibility of establishing a formal US subsidiary of PAION
- Member of Senior Management Team reporting directly to Chief Executive Officers
- Extensive involvement with collaborators and licensing partners including membership on joint steering committees
- Developed and implemented complete program plans identifying all critical path activities, resource constraints, and established budgets

Strategic Planning Consultant
Clinical and Regulatory Development
Elixir Pharmaceuticals (formerly Centagenetix) *(2002)*

- Focus on due-diligence review for product opportunities
- Evaluated potential in-licensing opportunity in cardiovascular disease
- Established development strategy (preclinical toxicology through NDA/MAA) for worldwide registration
- Contracted directly with CEO and CFO

Strategic Planning Consultant
Clinical and Regulatory Development
Windamere Venture Partners *(2001)*

- Focus on due-diligence review for funding opportunities
- Evaluated potential in-licensing opportunity in cardiovascular disease for funding
- Established development strategy (preclinical toxicology through NDA/MAA) for worldwide registration
- Consulted with inventor of technology to determine appropriate indications for registration

Pfizer (Warner-Lambert Company); Ann Arbor MI October 1990-March 2001
Pfizer is the world's largest global pharmaceutical research and development organization.

Director, Clinical Research, Oncology *(1999-2001)*

- Directed the global development program for an oncolytic replication-competent adenovirus (ONYX-015)
- Established and implemented worldwide Phase 2/3 registration strategy in multiple tumor types as well as developing and initiating exploratory Phase 1 trials
- Executed complete program plans and prospectively identified all critical path activities, bottlenecks, resource constraints, and budget issues and proposed solutions to deal with these constraints
- Extensive collaboration with the licensor, external consultants (domestic and international), cooperative groups, and the National Cancer Institute
- Successfully navigated process development, preclinical, clinical, regulatory, and marketing channels to ensure a smooth development pathway
- Supervised seven direct reports (Manager level and below)

Director, Clinical Research, Rheumatology and Immunology *(1998-1999)*

- Established the formation of the entirely new therapeutic group and recruited and supervised 10 direct reports (Study Managers and Clinical Research Associates)
- Developed and implemented the Phase 2/3 worldwide registration strategy for a novel symptomatic and disease-modifying small molecule for the treatment of rheumatologic disorders with a focus on rheumatoid arthritis and osteoarthritis
- Executed complete program plans and prospectively identified all critical path activities, bottlenecks, resource constraints, and budget issues and proposed solutions to deal with these constraints
- Collaborated with domestic and international consultants in rheumatology and drug-induced liver disease
- Successfully navigated process development, preclinical, clinical, regulatory, and marketing channels to ensure a smooth development pathway

Senior Manager, Worldwide Regulatory Affairs *(1994-1998)*

- Principal liaison with the following Divisions of FDA for Warner-Lambert products: Oncology Drug Products, Neuropharmacologic Drug Products, Cardiorenal Drug Products, Metabolism and Endocrine, Anti-inflammatory, Analgesic, and Ophthalmic Drug Products, Office of Orphan Drug Products
- Provided internal regulatory direction to drug development teams based upon interpretation of US and international regulations and regulatory guidance documents
- Led multidisciplinary teams in coordinating and executing key regulatory activities (IND and NDA task forces)
- Conducted multiple meetings (e.g., End-of-Phase 2 Meetings, Pre-NDA Meetings) to discuss regulatory strategy with several different divisions of the FDA.
- Primary point person in Worldwide Regulatory Affairs department regarding orphan drugs
- Responsible for coordinating the submission, filing, and subsequent negotiation of two large NDAs: Lipitor ® (atorvastatin calcium) for hyperlipidemia and suramin hexasodium for prostate cancer. Compiled and submitted multiple INDs to several divisions of CDER

Clinical Scientist, Clinical Central Nervous System / Gastroenterology
(1990-1994)

- Developed and conducted pivotal Phase 3 trials resulting in commercialization of Cognex (tacrine), the first drug approved for the treatment of Alzheimer's disease
- Initiated, managed, and summarized results from several Phase 2/3 clinical registration trials in dementia for NDA/MAA and publication in peer-reviewed journals
- Collaborated with marketing from Phase 2 through product launch; presented data to many large audiences (> 300) of physicians
- Evaluated potential in-licensing opportunities in dementia
- Prepared for and participated in FDA Advisory Committee Meeting for approval of tacrine
- Prepared for and attended CPMP Hearing for tacrine
- Organized review of tacrine hepatotoxicity including collaborating with international experts in hepatology

CURRICULUM VITAE

Name: Margaret J. (Knapp) Uprichard, Pharm.D.

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Sherborn, MA 01770

Contact Information: (508) 647-0706 (home)
(508) 333-1228 (cell)
(508) 647-5166 (fax)
muprichard@comcast.net

EDUCATION

Doctoral

University of Michigan (1984-1989)
College of Pharmacy
Ann Arbor, Michigan
Doctor of Pharmacy

Post-Doctoral

University of Michigan (1989-1990)
University of Michigan Medical Center
Ann Arbor, Michigan
Resident in Clinical Pharmacy

LICENSURE

State of Michigan Board of Pharmacy (1989)

PROFESSIONAL EXPERIENCE

2003-present

Sr. Vice President, Chief Development Officer *(2005)*
Sr. Vice President, Drug Development *(2004)*
Sr. Vice President, Clinical and Regulatory Affairs *(2003)*
Point Therapeutics, Inc
Boston, MA

2001-2003

President, Uprichard Consulting, LLC
Drug Development Consultant

Acting Vice President, Clinical and Regulatory Affairs
Curis, Inc.
Cambridge, MA
(2001-2002)

Head of Worldwide Regulatory Affairs and Preclinical Development
PAION, GmbH
Aachen Germany
(2002)

Strategic Planning Consultant
Clinical and Regulatory Development
Elixir Pharmaceuticals (formerly Centagenetix)
(2002)

Strategic Planning Consultant
Clinical and Regulatory Development
Windamere Venture Partners
(2001)

1999-2001 Director
Clinical Research, Oncology
Pfizer (Warner-Lambert Company acquired by Pfizer in June 2000)
Parke-Davis Pharmaceutical Research Division
Ann Arbor, Michigan

1998-1999 Director
Clinical Research, Rheumatology and Immunology
Warner-Lambert Company
Parke-Davis Pharmaceutical Research Division
Ann Arbor, Michigan

1994-1998 Senior Manager
Worldwide Regulatory Affairs
Warner-Lambert Company
Parke-Davis Pharmaceutical Research Division
Ann Arbor, Michigan

1990-1994 Clinical Scientist
ClinicalResearch
Central Nervous System/Gastroenterology
Warner-Lambert Company
Parke-Davis Pharmaceutical Research Division
Ann Arbor, Michigan

1996-2001 Pharmacist (Part-time)
Chelsea Pharmacy, Inc., Grass Lake, Michigan

1986-1996 Pharmacist (Part-time)
Saline Community Hospital
Saline, Michigan

ACADEMIC APPOINTMENTS

1989-present	Clinical Associate Professor of Pharmacy University of Michigan College of Pharmacy Ann Arbor, Michigan
1999-2001	Clinical Associate Professor of Pharmacy Ferris State University Big Rapids, Michigan

PROFESSIONAL ACTIVITIES *Regulatory Submissions*

NDA Submission: # 20-893, (suramin hexasodium)
Division of Oncology Drug Products (1997)

NDA Submission: # 20-702, Lipitor® (atorvastatin calcium)
Division of Metabolic and Endocrine Drug Products (1996)

IND Submission: hedgehog antagonist, July 2001
Division of Dermatologic Drug Products

IND Submission: intravenous kappa agonist, March 1995
Division of Neuropharmacological Drug Products

Orphan Drug Application – Hormone-Refractory Prostate Cancer: suramin hexasodium (1997) and Head Injury: intravenous kappa agonist (1996)

PUBLICATIONS IN PEER REVIEWED JOURNALS

1. *Knapp MJ,* Colburn P. Clinical uses of intravenous immune globulin. Clin Pharm. 1990;9:509-29.

2. *Knapp MJ,* Colburn P. Clinical uses of intravenous immune globulin. Am J Hosp Pharm. 1990;47:1878-84.

3. *Knapp MJ,* Berardi RR, Dressman JB, Rider JM, Carver PL. Modification of gastric pH with oral glutamic acid. Clin Pharm. 1991;10:866-9.

4. *Knapp MJ,* Berardi RR, Dressman JB, Rider JM, Carver PL. Modification of gastric pH with oral glutamic acid. Am J Hosp Pharm. 1991 December.

5. *Knapp MJ,* Jacobsen PA. Intravenous immune globulin therapy. Michigan Drug Letter. 1991:March.

6. *Knapp MJ,* Knopman DS, Solomon PR, Pendlebury WW, Davis CS, Gracon SI. A 30-week, randomized, controlled trial of high-dose tacrine in patients with Alzheimer's disease. JAMA. 1994;271:985-91.

***Publications in Peer Reviewed Journals** (continued)*

7. Watkins PB, Zimmerman H, *Knapp MJ*, Gracon SI, Lewis KL. Hepatotoxic effects of tacrine administration in patients with Alzheimer's disease. JAMA. 1994;271:992-8.

8. *Knapp MJ*, Gracon SI, Davis CS, Solomon PR, Pendlebury WW, Knopman DS. Efficacy and safety of high-dose tacrine: a 30-week evaluation. Alzheimer Disease and Associated Disorders. 1994;8:S22-31.

9. Knopman DS, *Knapp MJ*, Gracon SI, Davis CS. The Clinician Interview-Based-Impression (CIBI): a clinician's global change rating scale in Alzheimer's disease. Neurology. 1994;44:2315-2321.

10. Carver PL, Berardi RR, *Knapp MJ*, Rider MJ, Kauffman CA, Bradley SF, Atassi M. In vivo interaction of ketoconazole and sucralfate in healthy volunteers. Antimicrob Agents Chemother. 1994;38:326-9.

11. Green VJ, Pirmohamed M, Kitteringham NR, *Knapp MJ*, Park BK. Glutathione S-transferase mu genotype (GSTM1 0) in Alzheimer's patients with tacrine transaminitis. British Journal of Clinical Pharmacology. 1995;39:411-5.

12. Solomon PR, *Knapp MJ*, Gracon SI, Groccia M, Pendlebury WW. Long-term tacrine treatment in patients with Alzheimer's disease. Lancet. 1996;348:275-6.

13. Fontana RJ, Turgeon DK, Woolf TF, *Knapp MJ*, Foster NL, Watkins PB. The Caffeine Breath Test does not identify patients susceptible to tacrine hepatotoxicity. Hepatology. 1996;23:1429-35.

14. Gracon SI, *Knapp MJ*, Berghoff WG, Pierce M, DeJong R, Lobbestael SJ, Symons J, Dombey SL, Luscombe F, Kraemer D. Safety of tacrine: clinical trials, Treatment IND, and postmarketing experience. Alzheimer Disease and Associated Disorders. 1998;12:93-101.

15. Fontana RJ, deVries TM, Woolf TF, *Knapp MJ*, Brown AS, Kaminsky LS, Tang B-K, Foster NL, Brown RR, Watkins PB. Caffeine based measures of CYP1A2 activity correlate with oral clearance of tacrine in patients with Alzheimer's disease. Br J Clin Pharmacol. 1998;46:221-8.

16. Reid T, Galanis E, Abbruzzese J, Sze D, Wein LM, Andrews J, Randlev B, Heise C, *Uprichard M*, Hatfield M, Romel L, Rubin J, Kirn D. Hepatic arterial infusion of a replication-selective oncolytic adenovirus (dl1520). Cancer Research. 2002;62:6070-9.

17. Hamid O, Varterasian ML, Wadler S, Hecht JR, Benson III A, Galanis E, *Uprichard* M, Omer C, Bycott P, Hackman RC, Shields AF. Phase II Trial of Intravenous CI-1042 in Patients With Metastatic Colorectal Cancer. J Clin Oncol. 2003;21:1498-1504.

ABSTRACTS AND POSTER PRESENTATIONS

1. *Knapp MJ*, Berardi RR, Dressman JB, Rider JM, Carver PL. Modification of gastric pH with oral glutamic acid. Boston, MA. June 6, 1990. American Society of Hospital Pharmacists Annual Meeting.

2. Carver PL, Berardi RR, Rider JM, *Knapp MJ,* Kauffman CA. Interaction of ketoconazole and sucralfate in healthy volunteers. 30th International Conference on Antimicrobial Agents and Chemotherapy. Atlanta, GA. 1991: February.

3. Carver PL, Berardi RR, Rider JM, *Knapp MJ,* Kauffman CF. Interaction of ketoconazole and sucralfate in healthy volunteers. Ft. Lauderdale, FL. 1991: February. American College of Clinical Pharmacy Winter Meeting. Poster presentation.

4. Pendlebury WW, Davis DS, Gracon SI, *Knapp MJ*, Knopman DS, Solomon PR. Improved cognitive abilities in Alzheimer's patients receiving a high dose of tacrine. Society for Neuroscience. 1993;19:188;78.10. Abstract.

5. Fontana RJ, Turgeon DK, Woolf TF, *Knapp MJ*, Watkins PB. Tacrine hepatotoxicity: the use of caffeine to identify potential susceptibility factors. Hepatology. 1994;19:63I (104). Abstract.

6. *Knapp MJ*, Gracon SI. Tacrine: an overview of efficacy in multicenter clinical trials. Third International Springfield Symposium on Advances in Alzheimer Therapy. Springfield, IL. May 12-15. 1994. Abstract.

7. Fontana RJ, Turgeon DK, Woolf TF, *Knapp MJ*, Watkins PB. Tacrine hepatotoxicity: the use of caffeine to identify potential susceptibility factors. American Gastroenterological Association. New Orleans, LA. May 15-18, 1994. Abstract.

8. Gracon SI, *Knapp MJ*, Berghoff WG. Tacrine clinical trials: results of two parallel group studies. The Karolinska Institute Post-Graduate Education Series: Alzheimer's Disease - Advances in Research and Clinical Practice. November;1994. Abstract.

9. Solomon PR, *Knapp MJ*, Gracon SI, Groccia M, Kelly BB, Relin M, Pendlebury WW. Long-term tacrine treatment in patients with Alzheimer's disease. American Academy of Neurology. Washington DC. May 7-13, 1995. Abstract.

10. Lennox RD, McLaughlin-Miley C, Bohlig AM, Yan C, Scott-Lennox J, Jaffe M, *Uprichard M.* Measuring pain flare intensity in osteoarthritis research. Fourth World Congress of the Osteoarthritis Research Society International, Vienna, Austria. September 16-19, 1999. Abstract.

11. McLaughlin-Miley C, Lennox RD, Bohlig AM, Yan C, Scott-Lennox J, *Uprichard M,* Abitbol J-L. The impact of darbufelone on quality-of-life in osteoarthritis. Fourth World Congress of the Osteoarthritis Research Society International, Vienna, Austria. September 16-19, 1999. Abstract.

***Abstracts and Poster Presentations** (continued)*

12. Lane NE, Yan C, Hotary LH, McLaughlin-Miley C, *Uprichard MJ.* Placebo- and naproxen-controlled dose-ranging trial of darbufelone in osteoarthritis (OA). American College of Rheumatology 63rd Annual Scientific Meeting, Boston, MA. November 13-17, 1999. Abstract.

13. Schiff M, Bycott P, Kimmel K, McLaughlin-Miley C, *Uprichard MJ.* Placebo- and naproxen-controlled dose-ranging trial of darbufelone in rheumatoid arthritis (RA). American College of Rheumatology 63rd Annual Scientific Meeting, Boston, MA. November 13-17, 1999. Abstract.

14. Scheiman J, Abitbol J-L, Jaffe M, *Uprichard MJ.* Gastrointestinal safety of darbufelone in a randomized dose-ranging clinical trial versus placebo and naproxen in patients with rheumatoid arthritis. American College of Rheumatology 63rd Annual Scientific Meeting. Boston, MA. November 13-17, 1999. Abstract.

15. Nemunaitis J, Cunningham C, *Uprichard M,* Kirn D. Phase 1 dose-escalation trial of intravenous infusion of CI-1042 (ONYX-015) in patients with refractory cancer. Ninth International Conference on Gene Therapy. San Diego, CA. December 7-9, 2000. Abstract.

16. Nemunaitis J, Cunningham CC, Senzer NN, Haltom E, Jones, B, Rukelja SJ, Richards DA, *Uprichard MJ.* A phase 1 trial of PT-100 in patients receiving myelosuppressive chemotherapy. J Clin Oncol. Poster presented at the 39th Annual Meeting of the American Society of Clinical Oncology. New Orleans, LA. June 5-8, 2004.

17. *Uprichard MJ,* Jones B. Phase 1 rising single-dose study of talabostat (PT-100) in healthy volunteers. J Immunother. 2004;27:S17. Abstract #55. Poster presented at the 19th Annual Meeting of the International Society of the Biological Therapy of Cancer. San Francisco, CA. November 4-7, 2004.

18. Al-Katib A, Hurd DD, Raju R, Stephenson J, Giles F, Haltom E, *Uprichard MJ.* Phase 1 study of talabostat and rituximab in patients with indolent non-Hodgkin's lymphoma with primary resistance to or progression following rituximab. Blood. 2004;104:394a. Abstract #1403. Poster presented at the 46th Annual Meeting of the American Society of Hematology. San Diego, CA. December 4-7, 2004.

19. *Uprichard MJ,* Jones B. Phase 1 rising multiple-dose study of talabostat (PT-100) in healthy subjects. Blood. 2004;104(11);138b. Abstract #4215.

20. Cunningham C, Richards D, Salgia..., *Uprichard MJ.* Phase 2 trial of talabostat in patients with stage IIIB/IV NSCLC. J Clin Oncol. 2005;23:650s. Abstract #7120. Poster presented at the 40th meeting of the American Society of Clinical Oncology. Orlando, FL. May 14-17, 2005.

21. Redman BG, Ernstoff MS, Gajewski TF..., *Uprichard MJ.* Phase 2 trial of talabostat in stage IV melanoma. J Clin Oncol. 2005;23:727s. Abstract #7570.

22. *Uprichard MJ,* O'Day SJ, Pavlick AC et al. Phase 2 study of talabostat and cisplatin in stage IV melanoma. J Clin Oncol. 2005;23:725s. Abstract #7563.

23. Gajewski TF, Lawson DH, Redman BG..., *Uprichard MJ.* A Phase 2 study of talabostat in patients with Stage IV melanoma. J Immunother. 2005;28;627. Abstract. Poster presented at the 2005 Annual Meeting of the International Society of the Biological Therapy of Cancer. Alexandria, VA. November 10-13, 2005.

24. Cunningham C, Richards D, Salgia R..., *Uprichard MJ.* A Phase 2 study of talabostat/docetaxel in advanced NSCLC. Poster presented at the 2005 AACR-NCI-EORTC Annual International Conference. Philadelphia, PA. Nov 14-18, 2005.

25. Khan KD, O'Brien S, Rai KR..., *Uprichard MJ.* Phase 2 study of talabostat and rituximab in patients with advanced chronic lymphocytic leukemia (CLL) previously treated with a rituximab/fludarabine regimen. Blood. 2005;106(11);601a. Abstract #2125. Poster presented at the 47th Annual Meeting of the American Society of Hematology. Atlanta, GA. December 10-13, 2005.

BOOK CHAPTERS

Gracon SI, *Knapp MJ.* Tacrine: an overview of efficacy in two parallel group studies. In: Alzheimer disease: therapeutic strategies. Giacobini E, Becker R (eds). 1994;145-9. Birkhauser, Boston.

Gracon SI, Hoover TM, Lewis KW, Dolan-Ureno J, Rieger MM, Myers SL, *Knapp MJ.* Tacrine in Alzheimer's disease: efficacy and safety in a parallel-group study. Alzheimer's disease: advances in clinical and basic research. Corain B, Iqbal K, Nicoline M et al, eds. 1993;549-57. John Wiley & Sons Ltd.

INVITED PRESENTATIONS

Knapp MJ. Evaluation of a potential interaction between ketoconazole and sucralfate in healthy volunteers. Indianapolis, IN. April 7, 1990. Great Lakes Residency Conference.

Knapp MJ. Pharmacologic treatment of Alzheimer's disease. Springfield, MO. June 13, 1993. Midwest Neurology Conference.

Knapp MJ. A 30-week study of high-dose tacrine in patients with Alzheimer's disease. Berlin, Germany. September 9, 1993. International Psychogeriatric Association.

Knapp MJ. Report on tacrine clinical data. Charleston, SC. October 9, 1993. Merritt-Putnam Epilepsy Update.

Knapp MJ. Treatment of Alzheimer's disease with tacrine. Palm Beach Gardens FL. January 15, 1994. Conference: Medical Management of Alzheimer's disease.

Knapp MJ. Tacrine: an overview of efficacy in two parallel group studies. Springfield, IL. May 13, 1994. Third International Springfield Symposium on Advances in Alzheimer Therapy.

AWARDS AND HONORS

Martec Scholarship (1989)
Martec Pharmaceuticals

Regents' Scholarship (1984)
University of Michigan
Ann Arbor, Michigan

Calvin Scholarship (1984)
Edna Calvin Scholarship Fund
South Haven, Michigan

MEMBERSHIP IN PROFESSIONAL ORGANIZATIONS

American College of Clinical Pharmacy
American Society of Clinical Oncology
American Society of Hematology
Drug Information Association
Regulatory Affairs Professionals Society

PERSONAL REFERENCES

Available upon request

April 2006